Bloodborne Thrombin Promotes the Death of Murine Lymph Node Fibroblastic Reticular Cells

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Autoimmune diseases, including Rheumatoid Arthritis and Systemic Lupus Erythematosus, are characterized by symptoms of chronic tissue swelling and inflammation. It remains largely unknown what effect this chronic inflammation has on lymph nodes, the major sites of immune cell activation. During inflammation, increased leakiness in blood vessels leads to the death of lymph node fibroblastic reticular cells (FRCs) in mice (unpublished data). The objective of the research described herein was to confirm this phenomenon and to determine the components of blood that cause the death of FRCs. It was hypothesized that a) thrombin is the molecule in plasma responsible for the observed cell death and b) cells exposed to a combination of plasma and an inhibitor of the cellular thrombin receptor (Protease-Activated Receptor 1, or PAR1) will not exhibit a significant decrease in cell viability. FRCs were exposed to varying plasma dilutions to determine how much plasma is needed to cause significant cell death. FRCs were then treated with varying dilutions of plasma + PAR1 inhibitor. Finally, FRCs were treated with plasma + hirudin, a direct thrombin inhibitor from the salivary glands of leeches. Results show a rescue in plasma-treated FRCs in the presence of PAR1 inhibitor or hirudin. The data suggest that thrombin is one of the blood components extravasated during chronic inflammation that significantly decrease the viability of FRCs. The observed cell death could potentially hinder the ability of FRCs to facilitate the activity of other immune cells, such as B and T cells.

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